

Prognosis in Elderly Hypertensive Patients

Edward D. Freis

Department of Veterans Affairs Medical Center, Washington, DC, USA

Hypertension is the most common treatable disorder of the aged. The prevalence of hypertension is considerably higher in the elderly than in younger individuals. This is because blood pressure (BP), especially systolic BP, rises with age and, therefore, as people age, more develop hypertension. In the Hypertension Detection and Follow-up Program which screened 34 000 people between the ages of 60 and 69 years, 51% had a systolic BP > 140mm Hg and 42% had diastolic levels > 90mm Hg, a prevalence much greater than in younger persons (Curb et al. 1985). In addition, because of advances in healthcare a higher percentage of the population are now in the old age group. Further, the incidence of complications associated with hypertension is much higher in older than in younger patients. These complications include stroke, congestive heart failure, coronary artery disease (CAD), renal failure and aortic aneurysm. Lastly, and most importantly, treatment has been shown to reduce these complications.

This discussion will first review the prognosis of untreated hypertension in the aged and then will indicate how the outlook has changed since the introduction of antihypertensive drug treatment.

1. Prognosis Prior to Antihypertensive Drugs

The prognosis of mild to moderate hypertensive patients prior to the advent of antihypertensive drugs was reported in the 1941 publication of the Life Insurance Companies (Actuarial Society of

America 1941). Table I produced from this data shows that in people with systolic BP in the range of 108 to 132mm Hg, the ratio of actual to expected deaths was 58% higher in those with diastolic BP of 94 to 116mm Hg compared with those with diastolic BP between 59 and 83mm Hg. In people with diastolic BP in the range of 84 to 93mm Hg and systolic BP between 143 to 177mm Hg, mortality rose 47% compared with those with systolic BP between 133 to 142mm Hg.

A quantitative relationship was reported between arterial pressure and cardiovascular mortality over the whole range of arterial BP, both diastolic and systolic, from the lowest to the highest values. These data included all adult ages. In a later publication, the Metropolitan Life Insurance Company reported the 20-year follow-up in different age groups (Metropolitan Life Insurance Company 1961). In persons aged 50 to 59 years they found that BP of 138 to 147mm Hg (systolic) and 93 to 97mm Hg (diastolic) was associated with a mor-

Table I. Mortality ratios for cardiovascular disease [actual to expected deaths (expected = 100)] for all entry ages. (Actuarial Society of America and Association of Life Insurance Medical Directors 1941)

Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)		
	54-83	84-93	94-116
108-132	86	101	116
133-142	108	137	171
143-177	175	201	293

tality rate 1.7 times higher than in normotensive people.

Data from the Framingham and other studies in untreated older men with mild and moderate systolic and diastolic hypertension, indicate that for similar levels of BP the incidence of cardiovascular disease approximately doubles in elderly as compared with younger men (figs 1 & 2). The increase is less striking in older women (Vokonas et al. 1988).

Before antihypertensive drugs became available it was usual to find on the medical wards of general hospital patients with severe, including malignant, hypertension. These patients died within 1 to 2 years of renal failure, congestive heart failure, stroke or a combination of these complications. They showed an accelerated rise in diastolic BP which resulted in nephrosclerosis and further aggravated the hypertension causing a vicious cycle. Without treatment, diastolic BP reached 140 to 150mm Hg or even higher and was associated with

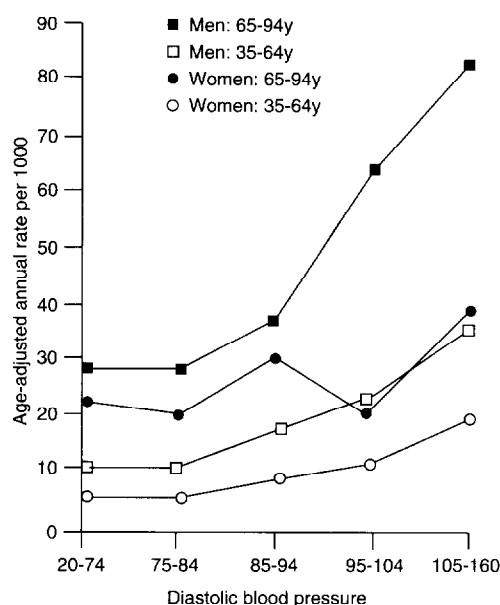


Fig. 2. Risk of cardiovascular disease by age, sex and diastolic blood pressure from a 30-year follow-up in the Framingham Study (from Vokonas et al. 1988, with permission).

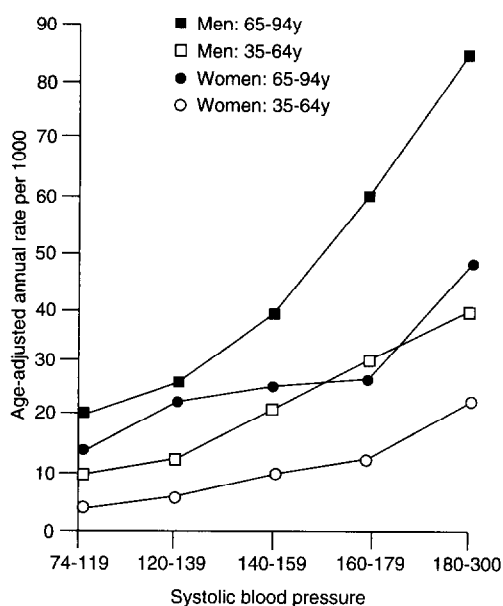


Fig. 1. Risk of cardiovascular disease by age, sex and systolic blood pressure from a 30-year follow-up in the Framingham Study (from Vokonas et al. 1988, with permission).

the appearance of neuroretinopathy, heralding the onset of fatal complications.

One of the most important prognostic features of untreated hypertension is its tendency to progress. As already indicated BP rises with age and, as a result, a high normal BP often rises into the hypertensive range. The Framingham study followed persons with normal (< 85mm Hg) [Leitschuh et al. 1991] and high normal (85 to 89mm Hg) diastolic BP over 26 years. The incidence of hypertension in the 85 to 89mm Hg diastolic group was between 2 to 3 times greater than in the < 85mm Hg group. The Framingham study (Leitschuh et al. 1990) found that the second leading risk factor associated with progression was gain in bodyweight over time. In the Veterans Administration Cooperative Study Group on Antihypertensive Agents (1970), approximately 2% of patients per year during follow-up of the placebo group (initial diastolic BP 90 to 114mm Hg) advanced to diastolic hypertension > 125mm Hg (Veterans Administration

Cooperative Study Group on Antihypertensive Agents 1970).

The incidence of CAD rises dramatically with combined elevated BP and high cholesterol in both sexes (Abbot & McGee 1987). In fact, the risk nearly triples compared with people with low normal values of both parameters (table II).

Left ventricular hypertrophy occurs in 20 to 40% of patients with mild hypertension as shown by the echocardiogram (Deveraux 1990). Furthermore, increased left ventricular mass diagnosed by echocardiogram is thought by some physicians to be a more precise prognostic indicator of hypertensive complications than BP itself (Koren et al. 1989; Levy et al. 1989). The prognosis is also greatly influenced by such complicating conditions as congestive heart failure, angina, renal impairment and diabetes mellitus.

To summarise, hypertension is extremely common in aged individuals. In untreated patients the risk of hypertension-associated complications, including progression to more severe hypertension, is greatly increased. The mortality rate in older hypertensive patients is approximately double that of younger patients for any given level of BP, either systolic or diastolic. Cardiovascular morbidity and mortality are directly related to the level of BP. Therefore, it is apparent that hypertension in the aged, including even mild systolic hypertension, particularly when combined with high cholesterol, left ventricular hypertrophy, diabetes mellitus or renal impairment is associated with excessive cardiovascular morbidity and mortality.

2. Change in Prognosis with Antihypertensive Drug Treatment

As recently as 10 years ago it was uncertain whether treatment of aged hypertensive patients with antihypertensive drugs would be effective and well tolerated. Since many of these patients have arteriosclerosis there was concern that many would experience hypotensive episodes that in themselves would lead to cardiovascular complications or at least to impaired function and quality of life. Recent evidence has shown, however, that these fears were unfounded and the prognosis has been greatly improved with carefully titrated treatment without impairing the quality of life (James & Potter 1993).

The first multicentre controlled trial to report the effects of antihypertensive drug treatment in patients age 60 years and older was that of the Veterans Administration Cooperative Study Group on Antihypertensive Agents (1972). The study showed a remarkable reduction in the incidence of stroke with drug treatment but no difference in the incidence of CAD. However, because of the relatively small numbers of patients entered, small differences might not have been detected.

A larger trial was carried out in Australia in elderly patients with baseline diastolic BP of 95 to 109 mm Hg (Management Committee of the Australian Therapeutic Trial in Hypertension 1981). The step-care treatment group began with chlor-thalidone to which various antihypertensive drugs could be added. Among patients aged 60 to 69 years there was a 39% reduction in cardiovascular

Table II. Probability per 1000 people of developing coronary heart disease in 8 years in 65 year old persons according to diastolic (DBP) and systolic (SBP) blood pressure and cholesterol levels [Data taken from the Framingham Study 26-year follow-up (Abbot & McGee 1987)]

Serum cholesterol levels (mg/dl)	Men			Women		
	DBP (mm Hg)			SBP (mm Hg)		
	80	90	100	120	150	180
185	107	130	166	49	71	103
235	128	154	184	59	89	122
285	151	181	215	71	101	144
335	178	212	251	84	120	169

Table III. Effect of antihypertensive drug treatment in placebo-controlled trials on cardiovascular morbidity and mortality in elderly patients. The incidence of strokes and coronary disease is given as % difference between the 2 treatment groups

Reference	Age (years)	Number of patients	Entry blood pressure (mm Hg)	Incidence of stroke (% difference)	Incidence of CAD (% difference)
Veterans Administration Cooperative Study Group on Antihypertensive Agents (1970)	>60	81	D 90-114	70	0
Management Committee of the Australian Therapeutic Trial in Hypertension (1981)	>60	582	D 95-109	33	18
EWPHE (Amery et al. 1985)	>60	840	S 160-239; D 90-119	32	38
SHEP Cooperative Research Group (1991)	>60	4736	S 160-219; D < 90	36	27
STOP (Dahlof et al. 1991)	>69	1627	S 180-230; D > 90. Or D 105-120 regardless of S	45	12
MRC Working Party (1992)	65-74	4396	S 160-209; D < 115	31 ^a	44 ^b

a These results apply to thiazide treatment which was significantly more effective than atenolol.

b All forms of cardiac deaths including congestive heart failure.

Abbreviations: CAD = coronary artery disease; D = diastolic BP; S = systolic BP.

complications. Compared with placebo, active treatment reduced stroke by 33% and CAD by 18%.

The European Working Party Trial (EWPHE) enrolled patients over the age of 60 years with BP of 160 to 239 mm Hg (systolic) and 90 to 119 mm Hg (diastolic) [Amery et al. 1985]. Using intention-to-treat analysis they found a reduction of 38% in cardiac deaths and of 32% in stroke mortality. The trial indicated a significant association between high systolic BP and cardiovascular morbidity and mortality.

The SHEP trial (Systolic Hypertension in the Elderly Program) was devoted entirely to the study of isolated systolic hypertension (SHEP Cooperative Group 1991). Treatment consisted mostly of chlorthalidone 12.5 to 25 mg/day. Drug treatment reduced the incidence of strokes by 36% compared with placebo. CAD events were reduced by 27% in chlorthalidone-treated patients.

The MRC (Medical Research Council of Great Britain) trial included 4396 elderly patients aged 65 to 74 years with mean systolic BP of 160 to 209 mm Hg during the pretreatment period (MRC

Working Party 1992). The patients were randomly assigned either to atenolol or hydrochlorothiazide plus amiloride or to placebo. Stroke and CAD events were significantly reduced only in the diuretic group. There was a nonsignificant trend towards a favourable outcome in the atenolol recipients.

The STOP-Hypertension trial (Swedish Trial in Old Patients) studied the effects of 3 β -blockers and a diuretic in 1627 patients aged 70 to 84 years (Dahlof et al. 1991). The criteria for entrance included an average systolic BP of 180 to 230 mm Hg with a diastolic BP > 90 mm Hg, or a diastolic BP of 105 to 120 mm Hg regardless of the systolic BP. Approximately equal numbers received active treatment (β -blockers or diuretic or both) or placebo. The incidence of stroke was significantly reduced. However, there was no essential difference in the incidence of myocardial infarction with either drug compared with placebo.

While all of these trials agree that the incidence of stroke is significantly reduced following treatment they differ with respect to the effects of anti-

hypertensive treatment on the incidence of CAD events. However, the consensus of the trials indicate that CAD is reduced although generally not as much as is stroke. While the Veterans Administration Cooperative Study Group on Antihypertensive Agents (1972) and STOP (Dahlof et al. 1991) trials reported essentially no difference in the incidence of CAD, the other 4 trials, including the 2 largest, found reductions with treatment (Management Committee of the Australian Therapeutic Trial in Hypertension 1981; MRC Working Party 1992; SHEP Cooperative Group 1991). Thus, the consensus indicated that there was success in preventing CAD events but it was less than in preventing stroke (table III).

An important but often overlooked benefit of treatment is the prevention of progression of hypertension to a more severe stage. In the various trials, except the Veterans Administration Cooperative Study Group on Antihypertensive Agents (1972) and STOP (Dahlof et al. 1991) trials, diastolic BP in the untreated patients averaged about or below 100mm Hg and if it rose to 110mm Hg the patients were treated. Therefore, the complications of severe hypertension were rarely encountered. Thus, treatment not only prevents stroke and to a lesser extent CAD but also by blocking progression to severe hypertension prevents the complications associated with such progression.

It is not the purpose of this paper to discuss types of drug treatment but it is worth noting that all of the therapeutic trials in the elderly used diuretics and stepped-care treatment. The SHEP Cooperative Group (1991) trial reported that their beneficial results were achieved '[w]ith the use of stepped-care treatment starting with low dose chlorthalidone as the step 1 medication which was increased if needed. With this once-per-day dosage the majority of treated patients were controlled at normal BP and with few adverse effects'. The concerns that have been raised regarding the safety of diuretics have now been mostly refuted (Freis 1989, 1992) and are far outweighed by the efficacy and low cost of these drugs. In my experience when diuretics fail, the addition of a second drug, espe-

cially a long acting angiotensin converting enzyme (ACE) inhibitor in low dosage, is usually highly effective and well tolerated in elderly patients.

Since the incidence of myocardial infarction is only partially prevented by antihypertensive drug treatment it follows that additional preventive measures should be taken including cessation of cigarette smoking, reducing saturated fat intake in diets, bodyweight reduction when indicated and regular exercise.

3. Summary

Hypertension is much more prevalent in the aged than in younger individuals and the risk of cardiovascular complications increases with age. Treatment of hypertension reduces this risk significantly. The benefits of treatment in improving prognosis are at least as striking in elderly as in young and middle-aged hypertensive patients.

References

- Abbot RD, McGee D. The probability of developing certain cardiovascular diseases in eight years at specified values of some characteristics. Framingham Study Section 37, NIH publication 87: 2284, 1987
- Actuarial Society of America and Association of Life Insurance Medical Directors (1941). Supplement to Blood Pressure Study. Actuarial Society of America and the Association of Life Insurance Medical Directors (Suppl. 234), New York, 1941
- Amery A, Brixko R, Clement D, DeSchaepe-dryver A, Fagard R, et al. Mortality and morbidity results from the European Working Party on High Blood Pressure in the Elderly. *Lancet* 325: 1349-1354, 1985
- Curb JD, Borhani NO, Schnaper H, Kase E, Entunste G, et al. Detection and treatment of hypertension in older individuals; the HDFP. *American Journal of Epidemiology* 121: 371-378, 1985
- Dahlof B, Lindholm LH, Hansson L, Schersten B, Ekblom T, et al. Morbidity and mortality in the Swedish trial in old patients with hypertension (STOP-Hypertension). *Lancet* 338: 1281-1285, 1991
- Devereux RB. Does increased blood pressure cause left ventricular hypertrophy or vice versa? *Annals of Internal Medicine* 112: 157-159, 1990
- Freis ED. Critique of the clinical importance of diuretic-induced hypokalemia and elevated cholesterol level. *Archives of Internal Medicine* 149: 2640-2648, 1989
- Freis ED. Adverse effects of diuretics. *Drug Safety* 7: 364-373, 1992
- James MA, Potter JF. The effect of antihypertensive treatment on the quality of later years. *Drugs & Aging* 3 (1): 26-39, 1993
- Koren MJ, Casale PN, Savage DD, Largah JH, Devereux RB. Relation of left ventricular mass to prognosis in essential hypertension. Abstract. *Circulation* 80 (Suppl. II): 538, 1989
- Leitschuh M, Cupples LA, Kannel WB, Gagnon D, Chobanian A. High normal blood pressure progression to hypertension in the Framingham Heart Study. *Hypertension* 17: 22-27, 1991
- Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Left ventricular mass and incidence of coronary heart disease in an elderly cohort. *Annals of Internal Medicine* 110: 101-107, 1989

- Management Committee of the Australian Therapeutic Trial in Hypertension. Treatment of mild hypertension in the elderly. *Medical Journal of Australia* 2: 398-402, 1981
- Metropolitan Life Insurance Company. Blood pressure: insurance experience. (A series of articles reprinted from the Statistical Bulletin, Metropolitan Life Insurance Company). Metropolitan Life Insurance Company, New York, 1961
- MRC Working Party. Medical Research Council trial of treatment of hypertension in older adults: principle results. *British Medical Journal* 304: 405-412, 1992
- SHEP Cooperative Research Group. Prevention of stroke by antihypertensive treatment in older persons with isolated systolic hypertension. *Journal of the American Medical Association* 265: 3255-3264, 1991
- Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effects of treatment on morbidity in hypertension. II. Results in patients with diastolic blood pressure averaging 90-114 mm Hg. *Journal of the American Medical Association* 213: 1143-1151, 1970
- Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effects of treatment on morbidity in hypertension III. Influence of age, diastolic pressure and prior cardiovascular disease; further analysis of side effects. *Circulation* 45: 991-1004, 1972
- Vokonas DS, Kannel WB, Cupples LA. Epidemiology and risk of hypertension in the elderly. The Framingham Study. *Journal of Hypertension* 6 (Suppl.): 53S-59S, 1988
-
- Correspondence and reprints: Dr *Edward D. Freis*, Department of Veterans Affairs Medical Center (151E), 50 Irving St, NW Washington, DC 20422, USA